

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner : Not yet assigned  
Group : Not yet assigned  
Applicants : Eric B. Kmiec, Howard B. Gamper and Michael C. Rice  
Serial No. : Not yet assigned  
Filed : Concurrently herewith  
For : TARGETED CHROMOSOMAL GENOMIC  
ALTERATIONS WITH MODIFIED SINGLE STRANDED  
OLIGONUCLEOTIDES

New York, New York  
March 27, 2001

Honorable Commissioner of Patents  
Washington, DC 20231

PRELIMINARY AMENDMENT

Sir:

Prior to issuing a first Office Action in the above-identified application, please amend the application as follows:

IN THE SPECIFICATION

Please replace page 1 of the application with substitute pages 1 and 1A submitted herewith\*.

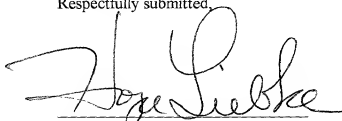
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\* An "Appendix of Amendments" is enclosed at Tab A showing the amendment to page 1. In the Appendix, the added portion is underscored.

REMARKS

Applicants have amended the specification to add reference to the priority claim which is also disclosed in the application filing documents. No new matter has been added. Entry of the amendment is requested.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Hope Liebke', written over a horizontal line.

Hope Liebke (Reg. No. 35,588)

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## TARGETED CHROMOSOMAL GENOMIC ALTERATIONS WITH MODIFIED SINGLE STRANDED OLIGONUCLEOTIDES

This application claims benefit from United States Provisional Application No. 60/192,176, filed May 27, 2000; United States Provisional Application No. 60/192,179, filed May 27, 2000; United States Provisional Application No. 60/208,538, filed June 1, 2000; and United States Provisional Application No. 60/244,989, filed October 30, 2000.

### Field Of The Invention

The technical field of the invention is oligonucleotide-directed repair or alteration of genetic information using novel chemically modified oligonucleotides. Such genetic information is preferably from a eukaryotic organism, i.e. a plant, animal or fungus.

### Background Of The Invention

A number of methods have been developed specifically to alter the sequence of an isolated DNA in addition to methods to alter directly the genomic information of various plants, fungi and animals, including humans ("gene therapy"). The latter methods generally include the use of viral or plasmid vectors carrying nucleic acid sequences encoding partial or complete portions of a particular protein which is expressed in a cell or tissue to effect the alteration. The expression of the particular protein then results in the desired phenotype. For example, retroviral vectors containing a transgenic DNA sequence allowing for the production of a normal CFTR protein when administered to defective cells are described in U.S. Patent 5,240,846. Others have developed different "gene therapy vectors" which include, for example, portions of adenovirus (Ad) or adeno-associated virus (AAV), or other viruses. The virus portions used are often long terminal repeat sequences which are added to the ends of a transgene of choice along with other necessary control sequences which allow expression of the transgene. See U.S. Patents 5,700,470 and 5,139,941. Similar methods have been developed for use in plants. See, for example, U.S. Patent 4,459,355 which describes a method for transforming plants with a DNA vector and U.S. Patent 5,188,642 which describes cloning or expression vectors containing a transgenic DNA sequence which when expressed in plants confers resistance to the herbicide glyphosate. The use of such transgene vectors in any eukaryotic organism adds one or more exogenous copies of a gene, which

gene may be foreign to the host, in a usually random fashion at one or more integration sites of the organism's genome at some frequency. The gene which was originally present in the genome, which may be a normal allelic variant, mutated, defective, and/or functional, is retained in the genome of the host.

Chemical	Formula	Weight	Concentration	Volume	Mass	Concentration	Volume	Mass
Hydrogen	$H_2$	2.016	1.000	1.000	2.016	1.000	1.000	2.016
Helium	$He$	4.003	1.000	1.000	4.003	1.000	1.000	4.003
Lithium	$Li$	6.941	1.000	1.000	6.941	1.000	1.000	6.941
Boron	$B$	10.811	1.000	1.000	10.811	1.000	1.000	10.811
Carbon	$C$	12.011	1.000	1.000	12.011	1.000	1.000	12.011
Nitrogen	$N_2$	28.014	1.000	1.000	28.014	1.000	1.000	28.014
Oxygen	$O_2$	31.999	1.000	1.000	31.999	1.000	1.000	31.999
Fluorine	$F_2$	38.001	1.000	1.000	38.001	1.000	1.000	38.001
Neon	$Ne$	20.180	1.000	1.000	20.180	1.000	1.000	20.180
Sodium	$Na$	22.990	1.000	1.000	22.990	1.000	1.000	22.990
Magnesium	$Mg$	24.305	1.000	1.000	24.305	1.000	1.000	24.305
Aluminum	$Al$	26.982	1.000	1.000	26.982	1.000	1.000	26.982
Silicon	$Si$	28.086	1.000	1.000	28.086	1.000	1.000	28.086
Phosphorus	$P_4$	123.895	1.000	1.000	123.895	1.000	1.000	123.895
Sulfur	$S_8$	256.536	1.000	1.000	256.536	1.000	1.000	256.536
Chlorine	$Cl_2$	70.906	1.000	1.000	70.906	1.000	1.000	70.906
Argon	$Ar$	39.948	1.000	1.000	39.948	1.000	1.000	39.948
Potassium	$K$	39.098	1.000	1.000	39.098	1.000	1.000	39.098
Calcium	$Ca$	40.078	1.000	1.000	40.078	1.000	1.000	40.078
Scandium	$Sc$	44.956	1.000	1.000	44.956	1.000	1.000	44.956
Titanium	$Ti$	47.883	1.000	1.000	47.883	1.000	1.000	47.883
Vanadium	$V$	50.942	1.000	1.000	50.942	1.000	1.000	50.942
Chromium	$Cr$	51.996	1.000	1.000	51.996	1.000	1.000	51.996
Manganese	$Mn$	54.938	1.000	1.000	54.938	1.000	1.000	54.938
Iron	$Fe$	55.847	1.000	1.000	55.847	1.000	1.000	55.847
Cobalt	$Co$	58.933	1.000	1.000	58.933	1.000	1.000	58.933
Nickel	$Ni$	58.693	1.000	1.000	58.693	1.000	1.000	58.693
Copper	$Cu$	63.546	1.000	1.000	63.546	1.000	1.000	63.546
Zinc	$Zn$	65.380	1.000	1.000	65.380	1.000	1.000	65.380
Gallium	$Ga$	69.723	1.000	1.000	69.723	1.000	1.000	69.723
Germanium	$Ge$	72.630	1.000	1.000	72.630	1.000	1.000	72.630
As	$As$	74.922	1.000	1.000	74.922	1.000	1.000	74.922
Se	$Se$	78.960	1.000	1.000	78.960	1.000	1.000	78.960
Br	$Br_2$	159.808	1.000	1.000	159.808	1.000	1.000	159.808
Krypton	$Kr$	83.801	1.000	1.000	83.801	1.000	1.000	83.801
Rubidium	$Rb$	85.468	1.000	1.000	85.468	1.000	1.000	85.468
Strontium	$Sr$	87.62	1.000	1.000	87.62	1.000	1.000	87.62
Yttrium	$Y$	88.906	1.000	1.000	88.906	1.000	1.00	

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